

~~Cancel Claim 18.~~

23. (Once Amended) A method for modulating the half life of a drug upon administration to a host, said method comprising:

a²
administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a half-life modulating moiety, wherein said bifunctional molecule has a modified half-life upon administration to said host as compared to a free drug control that comprises said drug;

Sub B¹
whereby the half life of said drug upon administration to said host is modulated as compared to a free drug control.

28. (Once Amended) A method for modulating the hepatic first-pass metabolism of a drug upon administration to a host, said method comprising:

a³
administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a hepatic first-pass metabolism modulating moiety, wherein said bifunctional molecule has a modified hepatic first-pass metabolism upon administration to said host as compared to a free drug control that comprises said drug;

whereby the hepatic first-pass metabolism of said drug upon administration to said host is modulated as compared to a free drug control.

~~Cancel Claims 33 to 50.~~

Please enter the following new claims:

a⁴
Sub B¹
--51. (New) A method for modulating at least one pharmacokinetic property of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a pharmacokinetic modulating moiety joined by a linking group, wherein said bifunctional molecule has at least one modulated pharmacokinetic property upon administration to said host as compared to a free drug control that comprises said drug;

whereby at least one pharmacokinetic property of said drug upon administration to said host is modulated as compared to a free drug control.

52. (New) The method according to Claim 51, wherein said pharmacokinetic property is selected from the group consisting of half-life, hepatic first-pass metabolism, volume of distribution and degree of blood protein binding.

53. (New) The method according to Claim 51, wherein pharmacokinetic modulating moiety binds to an intracellular protein.

54. (New) The method according to Claim 51, wherein said pharmacokinetic modulating moiety binds to an extracellular protein.

55. (New) The method according to Claim 51, wherein said drug target is a protein.

56. (New) The method according to Claim 51, wherein said bifunctional molecule is administered as a pharmaceutical preparation.

57. (New) A method for modulating the half life of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a half-life modulating moiety joined by a linking group, wherein said bifunctional molecule has a modified half-life upon administration to said host as compared to a free drug

control that comprises said drug;

whereby the half life of said drug upon administration to said host is modulated as compared to a free drug control.

58. (New) The method according to Claim 57, wherein said half-life modulating moiety binds to an intracellular protein.

59. (New) The method according to Claim 57, wherein said half-life modulating moiety binds to an extracellular protein.

60. (New) The method according to Claim 57, wherein said drug target is a protein.

61. (New) The method according to Claim 57, wherein said bifunctional molecule is administered as a pharmaceutical preparation.

62. (New) A method for modulating the hepatic first-pass metabolism of a drug upon administration to a host, said method comprising:

administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or an active derivative thereof and a hepatic first-pass metabolism modulating moiety joined by a linking group, wherein said bifunctional molecule has a modified hepatic first-pass metabolism upon administration to said host as compared to a free drug control that comprises said drug;

whereby the hepatic first-pass metabolism of said drug upon administration to said host is modulated as compared to a free drug control.

63. (New) The method according to Claim 62, wherein said hepatic first-pass metabolism modulating moiety binds to an intracellular protein.

64. (New) The method according to Claim 63, wherein said hepatic first-pass